Emerging Arboviral Infectious Diseases

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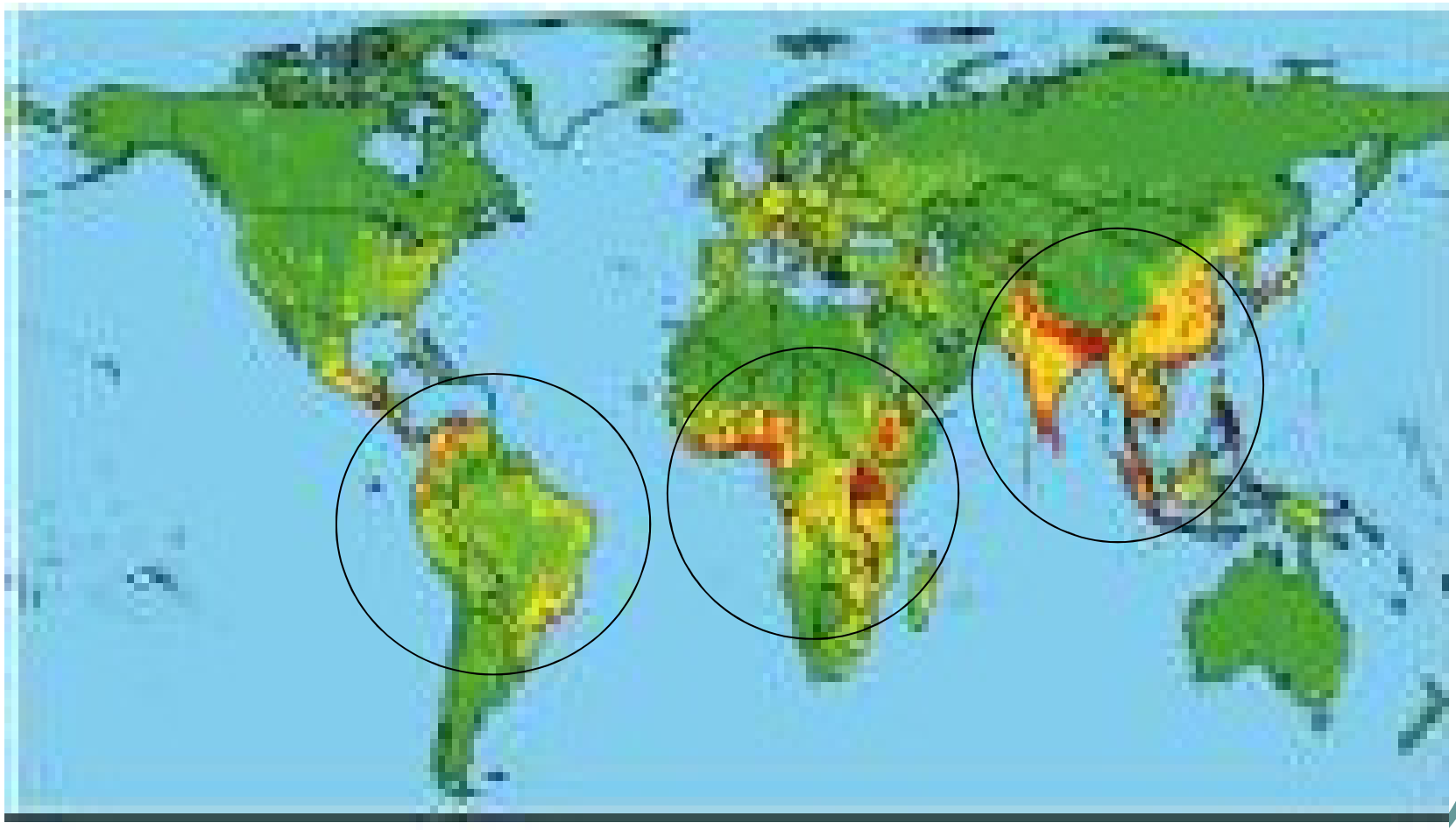
Presentation Overview

- Introduction- Emerging Infectious Diseases
- Emerging Arboviral Infections
- Examples of Emerging Arboviral Infections in India - Japanese Encephalitis, Chikungunya
- Vaccines against JE and Chikungunya in India
- Strategies to Control Arbovirus Infections

Hot Spots of Emerging Infections



Source: Jones et al, Nature

Factors Driving Incidence of EIDs

- Human demographics and behavior
- Technology and Industry
- Economic development and land use
- International travel and commerce
- Microbial adaptation and change
- Breakdown of public health measures
- Human vulnerability
- Climate and weather
- Changing ecosystems
- Poverty and social inequality
- War and famine
- Lack of political will
- Intent to harm

Source:Institute of Medicine 2003

Host Range and Emerging and Reemerging Infections

- 1407 Human pathogen species
- 177 (13%) species regarded as emerging or reemerging
- **Viruses: 208, and 77 (37%) emerging or reemerging**
- Bacteria: 538, and 54 (10%), respectively
- Fungi: 317, and 22 (7%), respectively
- Protozoa: 57, and 14 (25%), respectively
- Helminths: 287, and 10 (3%)

Source: Woolhouse MEJ et al, EID 2005; 11: 1842-47

Common Arboviruses

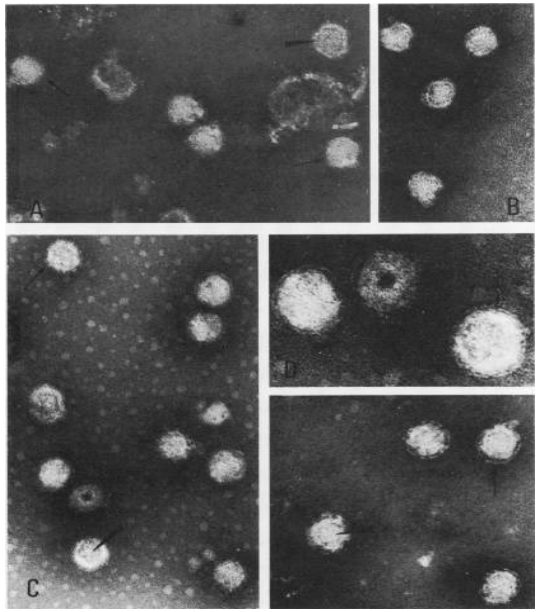
Family	Genera	Species (of high economic / epidemiologic importance)	Vectors	Diseases caused
Asfarviridae	Asfivirus	African swine fever virus	Tick	Viral encephalitis, viral hemorrhagic fever
Bunvaviridae	Phlebovirus	Rift Valley fever virus	Mosquito (*Aedes spp., Culex spp.*)	Viral encephalitis, viral hemorrhagic fever
Bunvaviridae	Phlebovirus	Pappataci fever, Toscana vrisu	Phlebotomus spp.	Fever
Bunvaviridae	Orthobunvavirus	California encephalitis virus	Mosquito	Viral encephalitis
Bunvaviridae	Nairovirus	Crimean-Congo hemorrhagic fever virus	Tick	Viral hemorrhagic fever
Flaviviridae	Falvivirus	Louping ill virus, Powassan virus, Tick-borne encephalitis virus	Tick (*Ixodes spp.*)	Viral encephalitis
Flaviviridae	Flavivirus	Dengue virus, Murray Valley encephalitis virus, Yellow fever virus	Mosquito	Viral encephaltiis, viral hemorrhagic fever
Flaviviridae	Flavivirus	Japanese encephaltiis virus, St. Louis encephalitis virus, West Nile virus	Mosquito	Viral encephalitis
Reoviridae	Coltivirus	Colorado tick fever virus	Tick	Viral hemorrhagic fever
Reoviridae	Orbivirus	African horse sickness virus, Bluetongue disease virus, Epizootic hemorrhagic disease virus	Ceratopogonidae (*Culicoides spp.*)	Viral encephalitis
Togaviridae	Alphavirus	Chikungunya virus, Eastern equine encephalitis virus, O'nyong'nyong virus, Ross River virus, Venezuelan equine encephalitis virus, Western equine encephalitis virus	Mosquito	Viral fever and encephalitis

3000 children died of JE since 2005 in UP alone.- NDTV 31, August 2010

JAPANESE ENCEPHALITIS

As many as 1589 people afflicted with JE in Gorakhpur, Basti and other districts of UP since January 2010. Of these 269 succumbed to the disease. – DNA, Sept 4, 2010

Japanese Encephalitis



Source: J.Virol. 1974

- A mosquito-borne flaviviral zoonotic infection
- Leading recognized cause of viral encephalitis in Asia
- Popularly called “Brain Fever”
- Approximately 3 billion people in Asia including 700 million children live in areas at risk for JE
- Most commonly infects children between the ages of 1 and 15 years and can also infect adults
- Causative agent: Arbovirus in the family Flaviviridae
- Spherical positive sense single stranded RNA virus
- 40-50nm diameter (approx)

Epidemiology and Transmission cycle

- Disease of rural, semi-urban, agricultural areas where vector mosquitoes proliferate in close association with pigs and other animal reservoirs.
- Seasonal disease - Epidemics coincide with monsoon and post monsoon
- Sporadic cases occur throughout the year in endemic areas
- 35000 to 50000 cases annually
- 20-30% case fatality
- 30-50% of the survivors have neurological sequelae
- Transmitted by mosquitoes (genera *Culex)*
- Pigs and ardeid birds most important hosts for maintenance, amplification and spread of the virus
- Vertical transmission in mosquitoes documented
- Human and horse –dead end host

Disease and Prevention

Disease

- A prodromal stage (Fever, Nausea, Vomiting)
- An acute encephalitic stage
  (Convulsions, unconsciousness, coma, Mask like face, stiff neck, muscular rigidity, tremors in fingers, eyelids, eye, tongue)
- A late stage characterized by persistence of signs of CNS, mental impairment, speech impairment, epilepsy and behavioral abnormalities

Prevention

- Vector control
- Vector avoidance
- Immunization of amplifying host
- Immunization of dead end host

Types of Vaccines

- Inactivated mouse brain derived vaccine
- Cell culture derived inactivated vaccine
- Cell culture derived live attenuated vaccine

Inactivated Vaccines

Inactivated mouse brain derived vaccine

- Derived from JE (Nakayama /Beijing-1 strain) virus grown in suckling mouce brain, inactivated with formalin
- Both Freeze dried and liquid formulation
- Use has been limited by cost, difficulty of production, and concerns over adverse reactions
- Varied sero-conversion rates, neutralizing antibody titers, and efficacy rates in different populations
- Adverse reactions: Neurological, hypersensitivity reactions & acute disseminated encephalomyelitis

Primary hamster kidney cells (PHK cells) derived inactivated vaccine

- P3 strain of JEV propagated on PHK cells, inactivated with formalin
- Needs repeated booster doses
- Efficacy ranged from 76-95%

Vero cell derived inactivated vaccine

- P3 strain based vaccine-licensed in china
- Beijing-1 based vaccine-under development in Japan
- SA14-14-2 strain based vaccine Purified, formalin inactivated and cultivated in Vero cells, Developed by US Army, produced by Intercell AG, Austria

Cell Culture Live Attenuated Vaccine

- Developed by Chinese scientists
- Virus strain-SA14-14-2
- Derived by passage through mice and tissue culture and produced in primary baby hamster cells
- Trials indicate high safety and immunogenicity
- 80-90% protection after single dose and 97.5% after two doses one year apart
- Doubts regarding its safety still inhibit wide spread use outside China and some other Asian countries

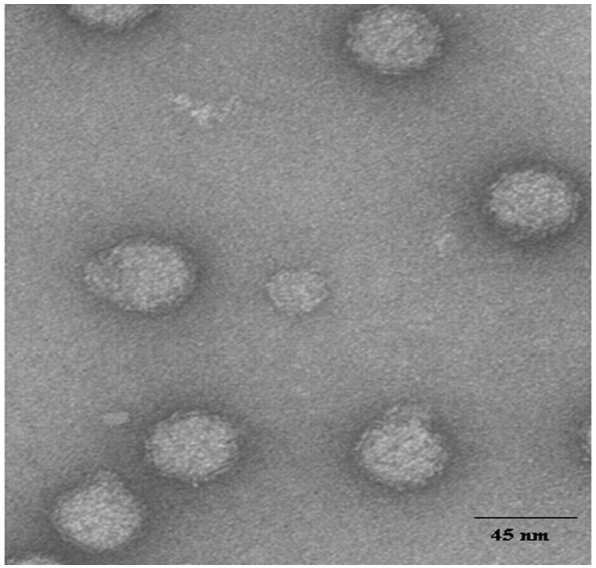
JE Vaccines in India

- **Central Research Institute, Kasauli manufactures mouse brain derived inactivated vaccine**
- **Indian Immunologicals Ltd.- Vero cell culture inactivated vaccine under development (Technology transfer from CDC, Taiwan)**
- **Biological E Ltd.- Inactivated vaccine under development (Collaboration with Intercell)**
- **Bharat Biotech Int. Ltd.- JE vaccine under development**
- **Panacea Biotech-Cell culture inactivated vaccine under development (Collaboration with National Institute of Immunology)**
- **Live vaccine imported from China currently used for immunization in India**

CHIKUNGUNYA

Five cases of Chikungunya reported in the municipal limits of Pune. This is the tip of iceberg. Most of the cases treated by private hospitals. – The Times of India, July 21, 2010

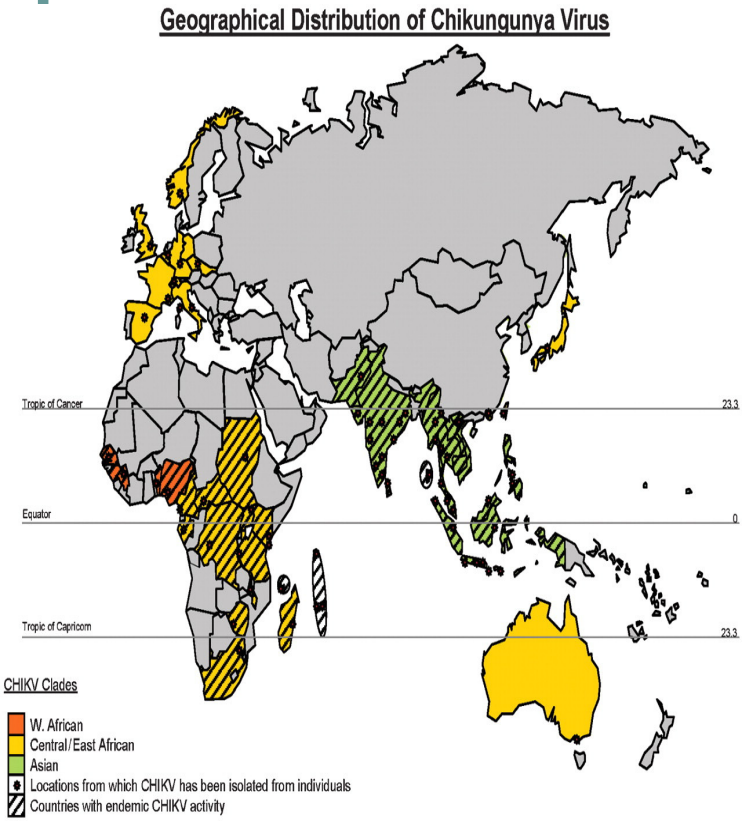
Chikungunya Fever



Source: Simizu et al 1984

- A mosquito-borne illness of human
- Characterized by arthritis mostly involving the wrist, ankle, knee and small joints of the extremities associated with rashes and fever
- Chikungunya virus affected millions of people in Africa, Indian sub-continent and Southeast Asia
- Causative agent : Chikungunya virus (CHIKV) of Togoviridae family and Alpha virus genus
- Linear positive sense single stranded RNA virus

Epidemiology and Transmission



- Chikungunya first described in Tanzania in1953
- Disease spread by Culicine and Aedes mosquitoes
- Believed to have originated from Africa where it has maintained in sylvatic cycle (wild primates and forest mosquitoes)
- Subsequently introduced in Asia
- During the 2005–2007 explosive epidemics on the Indian Ocean islands and in India
- Earlier out breaks- Kolkata 1963-64, Chennai 1965, Maharashtra 1973
- Transmitted by Culicine and Aedes mosquitoes
- Monkeys and other vertebrates act as common reservoirs
- In the epidemic period men also act as reservoirs
- Role of cattle and rodents also been reported in transmission
- CHIKV epidemics follows 3–4 year cyclical pattern that coincides with the repopulation of susceptible, non-immune, wild primates

Source: AM Powers et al J.Gen. Virol. 2007

Disease and Prevention

Disease

- A clinical triod of signs for CHIKV is ‘Fever, rashes and arthralgia’
- Sudden onset of fever reaching as high as 104^0F
- Fever always precedes the rash and joint pain
- Poly-arthralgia along with myalgia is a typical feature
- Infection is severe in infants, elderly and immunocompromised people
- Usually a self limiting disease but persons can develop chronic persistent and severe arthropathies
- Very few recorded fatalities

Prevention

- Vaccines not available
- Vector control
- Vector avoidance

Vaccines

- No commercial vaccine available
- Extensive development work carried out at US Army Research Institute, USA

  - Formalin inactivated vaccine-highly passaged strain

    (variable results on potency test)

  - Formalin inactivated vaccine-field isolated virus

  - Live attenuated vaccine (CHIK181/clone25)

    (phase 1 and 2 clinical trials were undertaken in naïve population
    98% developed neutralizing antibodies)

Chikungunya Vaccines in India

- Indian Immunologicals Ltd.- Live attenuated vaccine under development (Collaboration with US Army Research Institute of Infectious Diseases)
- Bharath Biotech International Ltd.- Vaccine under development

Challenges Faced by Vaccine Manufacturers

- Substantial expenditure on R&D
- Decision to invest in capacity and facility to be taken well in advance
- Large capital investment
- High investment costs and low ROI
- Long lead times for commercialization
- Unpredictability of demand

Primary Strategies to Control Arboviral Infections

Rural mosquito

Urban Mosquito

- Vector control
- Vector avoidance
- Mosquitocidal vaccines

Supporting Strategies to Control Vector Borne EIDs

- Epidemic preparedness and rapid response
- Vibrant public health infrastructure
- Effective communication
- Appropriate research and its utilization
- Political commitment

Summary

- Majority of emerging diseases caused by viruses
- Vector borne diseases require special attention
- Vector control crucial in controlling Arboviral infections
- Developing country manufacturers working on vaccines for emerging infectious diseases

Thank you